Brain cancers, such as glioblastoma multiforme (GBM), are heavily reliant on glucose and glutamine for the production of energy. Therefore, an approach to inhibit these fuels may reduce disease progression, essentially starving cancer cells. Calorically restricted ketogenic diet (KD) is a promising alternative in targeting energy metabolism because it decreases blood glucose and increases ketone levels. Additionally, high levels of glutamate in the brain frequently accompany GBM, causing excitotoxic neuronal death and an overall more negative prognosis for the patient. The need to reduce excess glutamate in GBM patients is the reasoning behind our proposed therapy with oxaloacetate (OAA). OAA is an important intermediate in the citric acid cycle, but it has been shown to serve as an effective blood glutamate scavenger and a mitochondrial biogenesis enhancer. In this experiment, we examined the combinatorial effects of restricted ketogenic diet (KGR) and OAA on the tumor growth and the survival rate for VM/Dk mice implanted with the highly metastatic VM-M3 tumor, a murine model for GBM.

We found KGR + OAA treatment has no influence on brain tumor size compared to mice treated only with KGR. However, mice treated with KGR + OAA live significantly longer than mice treated only with KGR. We also found that when hyperbaric oxygen treatment (O2) was used in conjunction with KGR + OAA, there was significantly less tumor growth compared to KGR or
KGR + OAA treatments. These preclinical findings show that metabolic cancer treatment combined with OAA could have therapeutic benefit for human GBM.